REMARKS/ARGUMENTS

By this Amendment, claims 50, 51, and 64 are amended. Claims 46-48, 50, 66-71, 74 have been withdrawn from consideration pursuant to a restriction requirement. Claims 38-57, 59-74 are pending. Claims 38-45, 49, 51-57, 59-65, 72-73 are under consideration.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2004/0265350.

Support for the amendments to the claims can be found throughout the Specification as filed, and specifically: support for the amendment to claim 64 for the limitations wherein the carrier comprises block hydroxyapatite and that the density of the carrier is less than about 30% theoretical can be found in ¶[0032], ¶[0058], ¶[0062], and ¶[0064].

Applicants hereby affirm their prior election with traverse of Group I, claims 38 to 73, and further elected the species chemotherapeutic agents, specifically MTX, reserving their rights under 35 U.S.C. § 121 to file a divisional application for the nonelected claims.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Rejection under 35 USC 102(b)

Claims 64 and 65 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Itokazu et. al. (J. Biomed. Mater. Res., 1998, 39, p. 536 - 538). This rejection is respectfully traversed.

The Examiner argues that independent claims 64 and 65 do not recite the identity of the ceramic carrier (i.e. does not distinguish between hydroxyapatite and ß-tricalcium phosphate or

any other ceramic). However, amended claim 64 requires a ceramic carrier comprising hydroxyapatite block having a density of less than 30% theoretical, i.e. a porosity of more than 70%. Hence, amended claim 64, and the claims dependent therefrom, are not anticipated by the disclosure of Itokazu, because Itokazu does not disclose each and every feature of the claim (i.e. a ceramic carrier comprising hydroxyapatite block having a density of less than 30% theoretical).

Accordingly, reconsideration and withdrawal of the rejection of claims 64 - 65 under 35 USC 102(b) is respectfully requested.

Claims 38 - 44, 51, 52, 61- 63, 72 and 73 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Imura et al. (US 6,340,648). This rejection is respectfully traversed.

The Examiner argues that the Imura reference teaches that a calcium phosphate porous sintered body, including hydroxyapatite, having pores of a size within the claimed range and a porosity of 55% or more and 90% or less (i.e. a theoretical density of 10 - 45%), which is allegedly anticipatory to applicant's ranges of less than about 30%, as in instant claim 38, or from about 10 to about 30%, as in instant claim 44.

In Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (MPEP 2131), the CAFC set forth that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". In the instant case, not every element of the claims is present in the Imura reference because while Imura discloses calcium phosphate porous sintered

bodies with a porosity of 55-90%, as regards hydroxyapatite bodies it discloses only articles having porosities of 65% (Example 3), 68% (Example 4) and 70% (Examples 1 and 2). This is outside the range required by instant claim 38, i.e. less than 30% theoretical density.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 - 44, 51, 52, 61- 63, 72 and 73 under 35 USC 102(b) is respectfully requested.

Claims 38 - 45, 59, 61 - 63, 72 and 73 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Smith et al. WO 98/15505. This rejection is respectfully traversed.

The Examiner argues that Smith discloses porous ceramic articles, and that the articles are preferably prepared from hydroxyapatite (page 8, line 17). The Examiner further alleges that Smith teaches that pore sizes may range from 50 - 150 microns or greater than 150 microns (page 8, lines 6 - 7 and claim 14), and that the pore sizes in the formed article can be controlled to yield a material with a pre-determined pore size and level of interconnectivity. The porosity may be from 20% to 90% (page 9, line 16). However, here, not every element of the claims is present in the Smith reference. The Smith reference does not teach an interconnected skeleton having pores the majority of which are in the range of from about 20 to about 800 micron, the carrier comprising block hydroxyapatite and having a density less than about 30% theoretical, wherein the pores contain a second material deposited therein, wherein the rate of release of the second material from the carrier is controlled.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 - 45, 59, 61 - 63, 72 and 73 under 35 USC 102(b) is respectfully requested.

Rejection under 35 USC 112 second paragraph

Claim 61 stands rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner argues that the claim is unclear because claim 38 defines the carrier as hydroxyapatite, however claim 61, which is dependent upon claim 38 broadens the carrier to include any metal or metal oxide. However, amended claim 61 recites that the carrier includes any non-metal oxide. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC 103(a)

Claims 38 - 45, 49, 51, 52, 61 - 65, 72 and 73 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Imura et al. (US 6,340,648) or Smith et al. WO 98/15505, in view of Itokazu et al. (J. Biomed. Mater. Res., 1998, 39, p. 536 - 538). This rejection is respectfully traversed.

The Examiner argues that it would have been obvious to one of ordinary skil in the art to utilize MTX as the drug which is deposited within the hydroxyapatite carriers of Imura or Smith, and that one would have been motivated to do so because Itokazu teaches similar chemotherapeutic agent loaded porous apatite ceramics to be useful to fill grafts after curettage of bone tumor, and one would have been motivated to utilize hydroxyapatite having a porosity within the claimed range as allegedly taught by Imura or Smith in order to achieve a carrier with an optimal balance of a desirable MTX release profile and adequate mechanical strength because

Imura and Itokazu both teach the importance of pore size and porosity in drug release and strength of the carrier

The claims are patentable over the combination of the Imura or Smith and Itokazu references for the following reasons. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991). MPEP 2143. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (KSR v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)).

Here, the Examiner admits that Imura or Smith do not specifically teach the identity of the drug which is delivered via the carrier. The Examiner alleges that Itokazu teaches porous apatite ceramics (PAC), including ß-tricalcium phosphate (TCP) and hydroxyapatite for the sustained release of a chemotherapeutic, methotrexate (MTX) (abstract), and that the MTX was

loaded into the pores of the ceramic carrier via centrifugation.

However, while Itokazu teaches the loading of a chemotherapeutic agent, MTX, into the pores of a porous apatite ceramic, only experiments with two types of porous apatite ceramic are discussed: hydroxyapatite block having a porosity of 35-48% and a pore size range of 50-300 μm; and ß-tricalcium phosphate block having a porosity of 75-80% and pore size range of 100-400 μm. In contrast, instant claim 38 requires a ceramic carrier comprising hydroxyapatite block having a density of less than 30% theoretical, i.e. a porosity of more than 70%. Hence, instant claim 38, and the claims dependent therefrom, are not anticipated by the disclosure of Itokazu, because Itokazu does not teach or suggest each and every feature of the claim (i.e. a ceramic carrier comprising hydroxyapatite block having a density of less than 30% theoretical).

In addition, while Imura discloses calcium phosphate porous sintered bodies with a porosity of 55-90%, as regards hydroxyapatite bodies it discloses only articles having porosities of 65% (Example 3), 68% (Example 4) and 70% (Examples 1 and 2). This is outside the range required by instant claim 38, i.e. less than 30% theoretical density. Consequently, Imura does not teach or suggest every limit of the claims.

In addition, the Smith reference does not teach or suggest an interconnected skeleton having pores the majority of which are in the range of from about 20 to about 800 micron, the carrier comprising block hydroxyapatite and having a density less than about 30% theoretical, wherein the pores contain a second material deposited therein, the rate of release of the second material from the carrier being controlled.

Therefore, the combination of the Imura or Smith and Itokazu references does not teach

or suggest every limitation of the claims. Since the combination of the references does not disclose or suggest all the limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 - 45, 49, 51, 52, 61 - 65, 72 and 73 under 35 USC 103(a) is respectfully requested.

Claims 38 - 45, 51 - 54, 56 - 57, 59, 61 - 63, 72, and 73 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Genin et al. (US 6,767,550), in view of Imura et al. (US 6,340,648) or Smith et al. (WO 98/15505). This rejection is respectfully traversed.

The Examiner alleges that Genin teaches a hydroxyapatite based drug delivery implant for cancer treatment, and that sustained release of the anti-cancer agents may be achieved after implantation at targeted sites. The Examiner further alleges that the Genin reference teaches that the ceramic component of the implant may be tricalcium phosphate, hydroxyapatite, etc.

However, Genin fails to identify the specific density of the ceramic used in the porous ceramic implant. This deficiency is not cured by the Imura reference. While Imura discloses calcium phosphate porous sintered bodies with a porosity of 55-90%, as regards hydroxyapatite bodies it discloses only articles having porosities of 65% (Example 3), 68% (Example 4) and 70% (Examples 1 and 2), this is outside the range required by instant claim 38, i.e. less than 30% theoretical density. In addition, the Smith reference does not teach an interconnected skeleton having pores the majority of which are in the range of from about 20 to about 800 micron, the carrier comprising block hydroxyapatite and having a density less than about 30% theoretical,

wherein the pores contain a second material deposited therein, the rate of release of the second material from the carrier being controlled.

Therefore, the combination of the Genin, Imura and Smith references does not teach or suggest every limitation of the claims. Since the combination of the references does not disclose or suggest all the limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 - 45, 51 - 54, 56 - 57, 59, 61 - 63, 72, and 73 under 35 USC 103(a) is respectfully requested.

Claims 38 – 45, 51- 57, 59, 61 - 63, 72, and 73 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Genin et al. (US 6,767,550), in view of Imura et al. (US 6,340,648) or Smith et al. WO 98/15505), in further view of Brem et al. (US RE 37,410). This rejection is respectfully traversed.

The Examiner alleges that Genin teaches a hydroxyapatite based drug delivery implant for cancer treatment. The Examiner further alleges that Imura discloses calcium phosphate porous sintered body which comprises spherical pores communicating with one another substantially throughout the body, and with a porosity between 55 - 90% (i.e. a theoretical density of 10 - 45%). (abstract). The Examiner further alleges that Smith discloses porous ceramic articles which are preferably prepared from hydroxyapatite and that Brem teaches biodegradable polymer matrices for the controlled local delivery of chemotherapeutic agents (abstract), and that examples of such biodegradable polymers include natural polymers such as

collagen, gelatin, etc. or synthetic polymers, preferably CPPSA.

The Examiner argues that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a ceramic with a density within the claimed range in the drug delivery implant of Genin consisting of drug-containing and drug-free layers because Imura or Smith teach porous calcium phosphate bodies, such as hydroxyapatite, to be useful for such purposes, and alleges that it would have been further obvious to substitute CPPSA for collagen as the bioresorbable material in the carrier of Genin because Genin teaches collagen .or bioresorbable polymers to be useful, and because Brem teaches that CPPSA is a biodegradable polymer which may be used as a functional equivalent to collagen.

However, Genin fails to identify the specific density of the ceramic used in the porous ceramic implant. While Imura discloses calcium phosphate porous sintered bodies with a porosity of 55-90%, as regards hydroxyapatite bodies it discloses only articles having porosities of 65% (Example 3), 68% (Example 4) and 70% (Examples 1 and 2). This is outside the range required by instant claim 38, i.e. less than 30% theoretical density. In addition, the Smith reference does not teach or suggest an interconnected skeleton having pores the majority of which are in the range of from about 20 to about 800 micron, the carrier comprising block hydroxyapatite and having a density less than about 30% theoretical, wherein the pores contain a second material deposited therein, the rate of release of the second material from the carrier being controlled. Additionally, the Brem reference does not teach or suggest the use of CPPSA biopolymers with a porosity of less than 30% theoretical density.

Therefore, the combination of the Genin and Imura or Smith, and Brem references does

not teach or suggest every limitation of the claims. Since the combination of the references does not disclose or suggest all the limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 – 45, 51- 57, 59, 61 - 63, 72, and 73 under 35 USC 103(a) is respectfully requested.

Claims 38 - 44, 51, 52, 59 – 63, 72 and 73 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Imura (US 6,340,648) in view of Hakamatsuka (US 5,318,779). This rejection is respectfully traversed.

The Examiner argues that it would have been obvious to one of ordinary skill in the art to include a collagen polymer on the porous calcium phosphate, including hydroxyapatite bodies of Imura having a porosity which is preferably in the range of 60 - 85% and pore size which is preferably from 100 – 4000 μm (column 2, lines 40 - 48) because such materials are allegedly useful as carriers for drug delivery and gradual release systems (column 1, line 9). The Examiner further argues that one would have been motivated to do so because Hakamatsuka specifically teaches that such an exterior coating layer can be used for further controlling release of a drug from a similar porous ceramic material.

However, as the Examiner admits, Imura does not teach coating the surface of the porous body with a polymer to further control release of the drug contained therein. In addition, the Hakamatsuka patent does not specifically teach that the ceramic is hydroxyapatite having a density of less than 30% theoretical. Therefore, the combination of the Imura and Hakamatsuka

references does not teach or suggest every limitation of the claims. Since the combination of the references does not disclose or suggest all the limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 38 - 44, 51, 52, 59 – 63, 72 and 73 under 35 USC 103(a) is respectfully requested.

* * *

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.